REMARKS

Claims 1-6 remain pending. Favorable reconsideration is respectfully requested.

An important feature of the claimed methods is that the negatively supercoiled DNA is detected ***in cells***. Since the DNA is detected in the cells, the claimed methods do not require extracting the DNA from the cells in order to be analyzed.

Sinden et al. teach that measurement of super-coiled DNA is possible by use of biotinylated psoralen. Although this reference describes a method of measuring super-coiled DNA, that method requires electrophoretic separation. Sinden et al. provides no evidence showing that the measurement of super-coiled DNA is possible in vivo as well.

Saffrin et al. teache a method of cross-linking biotinylated psoralen to DNA. However, the actual data related to such cross-links are no more than those obtained by an in vitro test, and this method requires that hybridization be carried out after DNA has been isolated.

Chevalier et al. describe in situ hybridization. However, there is no descriptive of using biotinylated psoralen in that reference.

Compared with the cited references above, the present invention provides a novel method for detecting negatively supercoiled DNA in living cells, which is characterized by visualizing negatively supercoiled DNA in living cells. This method, as described in the present specification, makes it possible to detect any fragment of negatively supercoiled DNA which would never have been possible to detect if its detection is carried out by a classical method using the hybridization technique. Therefore, the method of the present invention cannot be predicted whatsoever by one skilled in the art.

This is because the classical methods are inevitably required to take a hybridization step for probe, so that the overall system of a genome becomes too hard to detect. By contrast, the method of the present invention makes it possible to visually detect any super-coiled DNA contained in the overall system of a living cell.

Indeed, the method thus accomplished by the present invention is bringing many benefits to this medical field. For instance, it has become possible to discriminate between human leukemia cells and leukocytes, thanks to the method of the present invention. A Rule 132 Declaration which describes such an experiment will be submitted shortly.

Sinden et al. is a scientific literature reviewing the use of psoralen, and it has long been known that psoralen is cross-linked to negatively supercoiled DNA by hybridization, as mentioned in Reference 2 (Sinden, R.R., Carlso, J.O., and Pettjoh, D.E. (1980) Cell 21, 773-783) cited by Sinden et al. In contrast, the claimed method, characterized by the visualization of negatively supercoiled DNA in living calls, has never been has never been described before. This indicates that the method of the present invention would have been non-obvious to one skilled in the art.

In view of the foregoing, withdrawal of this ground of rejection is respectfully requested.

Applicants submit that the present application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon

James J. Kelly, Ph.D.
Attorney of Record
Registration No. 41,504

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 06/04)